REMARKS

Applicant respectfully requests reconsideration of the present application in view of the reasons that follow.

Status of claims

Claims 12-18 are pending in the application.

Claims 1-11 are canceled.

Enablement Rejection

Claims 12-18 were rejected, under 35 U.S.C. § 112, first paragraph, because the specification is allegedly not enabling for a method of treatment or prophylaxis of chronic fatigue syndrome (CFS). Office Action of August 26, 2004 at paragraph (¶) 5. The rejection is traversed because the specification clearly provides such enablement.

A. CHS versus CFS

The Office Action, at ¶ 5, acknowledges that the specification *is enabling* "for a process of decreasing expression of one or more inflammatory cytokines IFN-γ and IL-6." The specification explicitly identifies CFS as "a disorder associated with excessive amounts of one or more of the inflammatory cytokines IFN-γ and IL-6." Page 2, lines 23-28. The specification further provides a series of references in support of this teaching (*e.g.*, bottom of page 9). Evidence of record admits that there are likely other factors involved in CFS but this admission does not negate the efficacy of the claimed invention – many disease have complex etiologies.

Since the methods for treating a disease associated with excessive amounts of one or more of the inflammatory cytokines IFN-γ and IL-6 are the same, regardless of the particular disease, it is immaterial that the example used in the specification is the treatment of CHS rather than CFS. According to the Patent Office's own M.P.E.P. at 2164.02

> [t]he presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure . . . [t]o make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims.

Here, there is no reason that one could not extrapolate the methods of treatment of CHS to that of CFS because the underlying method for treatment is the same for these two disorders because the underlying causation, *i.e.*, the expression of excessive amounts of one or more of the inflammatory cytokines IFN-γ and IL-6, are, at least in part, the same.

The Office Action cites the alleged need for undue experimentation as a reason for the enablement rejection (*e.g.*, bottom of page 4). However, there are many factors to be considered in making a rejection based on undue experimentation. *In re Wands*, 858 F.2d 731,737 (Fed. Cir. 1988) One of them is the *nature* of the invention, which appears to have been overlooked by the Patent Office. *Id.*

Here, the *nature* of the claimed invention is that readministered, extracorporeally-stressed blood provides beneficial effects that transcend a single disease, such as CHS. Because reintroduction of stressed blood produces changes in cytokine levels, the methods of the invention is useful for treating a number of diseases *without additional modification.* This is an important consideration because it means that the need for experimentation is minimal. One skilled in the art need only follow the guidance provided for the treatment of CHS to treat CFS.

The standard for enablement is whether "one reasonably skilled in the art could make or use the invention . . . without undue experimentation." *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1384 (Fed. Cir. 1986). Here, by simply following the guidance provided in the specification with respect to CHS one skilled in the art could to apply the invention to CFS. There is minimal *experimentation* necessary.

In stating that "is would take undue trials and errors to practice the claimed invention" (bottom of page 4), the Office Action appears to be equating its apparent skepticism of the

success of the invention in treating CFS with the undue experimentation standard for compliance with the enablement requirement. This is a misapplication of the law. Even if, *arguendo*, the claimed invention did not prove effective in treating CFS (which Applicants expressly do not concede) it would not require undue experimentation to make this determination. Once need only follow the CHS example in the specification and monitor the progress of the CFS patient. Applicants submit that there is no undue experimentation required.

B. Prophylaxis versus Treatment

The Office Action at page 4 (first full paragraph) alleges that the specification is not enabling for methods of prevention/prophylaxis, as opposed to treatment. However, methods of prevention, as well as treatment, are enabled by the specification. The specification states, at the bottom of pages 2 and 9, that "the invention is useful in the medical treatment of patients suffering from, *prone to, or at risk of contracting* a disorder associated with excessive amounts" of IFN-γ and IL-6 (emphasis added). The methodology for treatment is the same as that for prophylaxis, which is fully disclosed in the specification. Moreover, there would appear to be no basis for distinguishing between *treatment* and *prophylaxis*, in terms of compliance with the enablement requirement.

The rejection appears to add a layer of complexity to the prophylactic use of the invention in stating that "the specification does not provide guidance . . . [for] . . . screening those patients susceptible to any inflammatory disease." *Supra.* To the extent that any screening would be required to practice the invention for prophylaxis, such screening is readily apparent from reading the specification. Such individuals would present with increased levels of the cytokines that the claimed methods are disclosed to reduce. The levels of these cytokines are clearly measurable since they are measured in the Example and are the subject of Figures 1 and 2. Thus prophylaxis/prevention, as well as treatment, of disorders associated with excessive levels of IL-6 and IFN-γ, are enabled by the specification, or by the specification combined with the knowledge of those skilled in the art.

C. Animal models and undue experimentation

The Office Action asserts that there is no animal model for CFS and that it would be unpredictable how to correlate the data obtained in mice with *in vivo* results. ¶ 5 (bottom of page 3).

At the outset, Applicants note that experiments in mice are *in vivo* results. The question relevant to the enablement issue must, therefore, be whether the *in vivo* results obtained in treating CHS in mice are applicable to the *in vivo* treatment of CFS in humans. Applicants have already addressed the issue of CHS v. CFS. The remaining question is whether the description of the treatment of mice is enabling for the treatment of humans. If it is not, countless issued U.S. patents should be withdrawn from issue. U.S. Patent law has never required the disclosure of studies in humans to support claims drawn to the treatment of humans.

D. Conclusions with respect to the enablement rejections

Applicants submit that the Patent Office has disguised its skepticism of the *utility* of the claimed invention as an *enablement* rejection, relying heavily on the "undue experimentation" standard applied to questions of enablement. However, the phrase "undue experimentation" does not encompass "skepticism."

The specification describes a methods for stressing and reintroducing blood, which is then useful for treating a variety of disorders, including CHS and CFS. Since practicing the claimed invention in treating CHS or CFS require the same procedure, it is simply incorrect to assert that undue experimentation is necessary.

Claims 12-18 are fully supported in the specification and the outstanding enablement rejection should be withdrawn.

Obviousness rejection

Claims 12-18 were rejected under 35 U.S.C. § 103 as allegedly being obvious over WO 98/07463, U.S. Patent No. 5,980,954, or WO 00/06703 in view of a certain CDC Report.

The Office Action states at page 6, ¶ 7, that an obviousness rejection cannot be overcome by attacking the references individually. However, this rule of patent law does not insulate an obviousness rejection from attack. Patent law has never precluded an Applicant from arguing against a combination of references, based on the teachings of the individual references. Here, the traversal is on the grounds that one skilled in the art would not be motivated to combine the cited references.

The Office Action at page 7 (first full paragraph) acknowledges that "the above references are silent about the fact that [the] disease condition in a patient is mediated by excess inflammatory cytokine production . . . *i.e.*, IL-6." This statement is important because it is largely the association of CFS with elevated levels of IL-6 and IFN-γ that make the methods of the invention applicable to treating/preventing CFS. It is therefore unclear, from the language of the rejection, why one skilled in the art would be motivated to use the methods of the cited references to treat CFS, absent the teachings of the present application.

The Office Action appears to assert that the disclosure, in the instant application, of the mechanism by which the claimed invention would treat/prevent CFS does not distinguish the instant application from the cited references. This is clearly not true. This disclosure links the methods involving stressed autologous blood to the disease that is subject of the claims.

In the absence of this disclosure, one skilled in the art must rely on some other reference to make the connection between the administration of stressed autologous blood and CFS. With respect to the outstanding obviousness rejection, the CDC reference must fulfill this role. Yet, the CDC reference does not teach that "CFS is an inflammatory disease mediated by excess inflammatory cytokine production," at stated in the Office Action at page 7 (third paragraph from

bottom). The CDC article list a number of "Possible Causes" for CFS (*i.e.*, "Virus," Immune Response," "Infection and Inflammation," Endocrine System," Chemical Sensitivity," Mental Sensitivity," and Oxidative Stress"). Pages 6-7. While the CDC article discusses inflammatory cytokines in the context of "[a] theory published by Dr. Martin L. Pall," (page 10), the article does not adopt this theory. It merely present it as one of several theories that may explain CFS. Moreover, if the CDC article can be said to adopt any particular theory, it is one that involves viral infection, wherein a component of a treatment for CFS is treating the underlying viral infection. Page 10 and elsewhere.

In re Vaeck requires the Patent Office to show some motivation for combining references to support an obviousness rejections. 947 F.2d 488 (Fed. Cir. 1991). Here, the prior art references, which can allegedly be combined to render the instant invention obvious, clearly operate under different theories of disease etiology. It is not clear why one skilled in the art would combine the speculative CDC reference, which primarily dealt with CFS as a disease causes by a virus, with two references that disclosed methods for modulating immune function with autologous stressed blood. There is no nexus to connect these references and motivate one skilled in the art to make the combination.

Note that in traversing the rejection, Applicants are not "attacking" the individual, substantive teachings of the references. Applicants are identifying what is taught by the references and asserting that one skilled in the art would not be motivated to combine them. The mere fact that references can be combined is not sufficient to support an obvious rejection. *In re Mills*, 916 F.2d. 680 (Fed. Cir. 1990). Here, the Patent Office has failed to establish any basis for making the combination.

For the reasons discussed herein, and other reasons presented during the prosecution of the application, Applicants submit that the Patent Office has failed to establish a prima facie case for obviousness and that the outstanding obviousness rejection must be withdrawn.

Notice of Appeal

While Applicants believe the present application is in condition for allowance, a Notice of Appeal has been filed to avoid the unintended abandonment of the application at the six-month date following the mailing of the most recent Office Action.

CONCLUSION

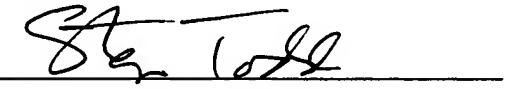
Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date: January 18, 2005

By 

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